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METHOD FOR THE NEOGENESIS OF CELL AGE (PCT/JP00/03917)

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The field of my invention

This invention belongs to the field of biology and life science.

Past ways of thinking

So far, all creatures were thought to grow old and to die.

The point of my invention

This invention prevents ageing and maintains good functions of individuals, organs, tissues, and cells for a long time. In order to achieve this purpose, my invention produces new cells from creatures whose ageing has progressed. With these new cells, I can newly regenerate cells, tissues, organs, etc. Thus, this invention is repetition of the exchange process of aged cells, tissues, and organs for newly–regenerated cells, tissues, and organs.

Concise explanations of my inventive figures

The first figure shows germ–line cells of individuals and clone bodies used for regeneration of clone bodies, organs, tissues, cells, etc., which have new cell age. 1 the male. 2 the female. 3 duplicating process by mitotic division (mitosis). 4 developing process. 5 first meiotic division. 6 second meiotic division. 7 primordial germ cells. 8 spermatogonia. 9 primary spermatocyte. 10 secondary spermatocytes. 11 spermatids. 12 transformation (spermiogenesis). 13 mature sperm cells (spermatozoa). 14 primordial germ cells. 15 oogonia. 16 primary oocyte. 17 first polar body. 18 secondary oocyte. 19 second polar body. 20 ovum.

The second figure shows new clone bodies generated from individuals and original clone bodies, by use of somatic cells including 2n germ cells, use of diploid, use of cell fusion, etc. The second figure also shows newly–regenerated clone body groups made from groups of individuals and these clone bodies by fertilization, parthenogenesis, etc. This figure indicates the practical use systematically of variously leveled many clone body groups, with excelling beyond generations. 21 somatic cells. 22 diploid. 23 cell fusion. 24 clone bodies. 25 parthenogenesis. 26 fertilization. 27 newly–regenerated clone bodies. 28 newly–regenerated clone body groups.

The effective method of my invention

This invention regenerates clone bodies, organs, tissues, cells, etc., which have new cell age, from germ cells of individuals and clone bodies of all creatures. I will explain this invention in detail, according to appended figures.

To begin with, as Fig.1 shows, nuclei of primordial germ cells 7, spermatogonia 8, primary spermatocytes 9, in the male 1, primordial germ cells 14, oogonia 15, primary oocytes 16, in the female 2, which have 2n diploid generation in individuals and clone bodies of creatures, are transplanted by cell fusion into the non–fertilized egg of which polar bodies and chromosomes were removed. And I regenerate new cell age clone

bodies, organs, tissues, cells, etc., by this means. Then I exchange old bodies, organs, tissues, cells, etc., for these new ones.

When these above mentioned cells in the male 1 are hard to gather, I make 2nXY cell nuclei by cell–fusing 23 nX state of secondary spermatocytes 10, spermatids 11, spermatozoa 13, and nY state of secondary spermatocytes 10, spermatids 11, spermatozoa 13, by surfactants, Sendai virus, etc., and as well, at the stage from primary spermatocytes 9 to secondary spermatocytes 10, by acting with antimitotic drugs such as colchicine, vinca alkaloids, taxol, and by temperature treatment, etc.

When these above mentioned cells in the female 2 are hard to gather, I make diploid 22 cell nuclei by cell–fusing 23 both of secondary oocytes 18, ova 20, polar bodies 17 19, by surfactants, Sendai virus, etc., and as well, at the stage before the first polar body 17 appears from the primary oocyte 16, at the stage before the second polar body 19 appears from the secondary oocyte 18, at the stage before the first polar body 17 divides into two second polar bodies 19, by acting with antimitotic drugs such as colchicine, vinca alkaloids, taxol, and by temperature treatment, etc.

In the case that I produce female clone bodies 24 from male individuals and clone bodies 24 in Fig.2, I make diploid 22 cell nuclei by cell–fusing 23 both of nX state of secondary spermatocytes 10, spermatids 11, spermatozoa 13, by surfactants, Sendai virus, etc., and as well, at the stage from nX state of secondary spermatocytes 10 to spermatids 11, by acting with antimitotic drugs such as colchicine, vinca alkaloids, taxol, and by temperature treatment, etc.

From these clone bodies generated in this way, I can regenerate repeatedly above mentioned clone bodies, organs, tissues, cells, etc., by using these somatic cells and germ cells. Furthermore, I get newly–regenerated cells with completely recovered telomeres by fertilizing 2nXY clone bodies and 2nXX clone bodies. In these newly–regenerated clone body groups 28, I can get infinite newly–regenerated cells by using fertilization 26 together in addition to use of somatic cells 21 including 2n germ cells, use of diploid 22, use of cell fusion 23, etc.

Moreover, in 2nXX clone body 24 groups, I can make use of somatic cells 21 including 2n germ cells, use of diploid 22, use of cell fusion 23, etc. In these ways I can also produce eggs of 2nXY and 2nXX, in groups of 2nXY and 2nXX, and in groups of 2nXX. And then I can develop by using the place of eggs, like haploid phase parthenogenesis such as ants, honeybees, and diploid phase parthenogenesis such as aphids, water fleas, etc. In brief, eggs originally have the capacity of development. And so I can operate artificial parthenogenesis by brushing eggs, by treatment of eggs with butyric acid and hypertonic seawater, by pricking eggs with bloody needles and sharp needles, etc., like parthenogenesis of creatures such as silk moths, sea urchins, frogs, Leporidae, etc. Thus I can make newly–regenerated clone body groups 28 of 2nXY and 2nXX, and newly–regenerated clone body groups 28 of 2nXX. In these groups, I can get infinite newly–regenerated cells by using parthenogenesis 25 together in addition to use of somatic cells 21 including 2n germ cells, use of diploid 22, use of cell fusion 23, etc. Not only using asexual reproduction and sexual reproduction together but also making the most of variously generated clone bodies as systematical groups beyond generations brings about great benefits to all the creatures for maintaining rejuvenated new individuals, organs, tissues, cells, etc. Besides, I can resurrect ancient creatures, by joining crossable and fertile closely–related species to one side of newly–regenerated clone body groups, and as well, by creating generations such as female germ cells from crossing newly–regenerated clone bodies and preserved DNA, RNA, germ cells, etc., and by repeated processes crossing these newly regenerated generations such as female germ cells with these closely–related species, preserved DNA, RNA, germ cells, etc., which have been maintained for so long in this world. When there are creatures which can reproduce by virgin development, I resurrect these creatures artificially by parthenogenesis with physical and chemical treatments.

Alternation of diploid and haploid phases and zygoses are the points of rejuvenation in cells. Creatures, such as green algae, developing

haploid n phase, form diploid 2n zygotes and rest, when the environment for asexual reproduction by cell division gets worse. And in spring these creatures undergo meioses to produce haploid n generations and form holdfast cells which anchor the plant and initiate growth. However, evolution directs retrogression of n generations and progress of 2n generations. Lots of creatures completely regenerate telomeres, which are said to be lost as getting older, by conjugation of both n generations created by meioses of 2n generations. And, in virgin development, haploid n generations and diploid 2n generations, as they are, obtain perfect telomeres by the place of eggs. In germ–line cells telomerases maintain the length of telomeres. Individuals preserve vigorously–dividing cells like hematogenous cells, which also have slight telomerase activity. However, ordinary somatic cells are deficient in telomerase activity. Thus, in order to keep the life span of cells, tissues, organs, etc., making telomerases work forcibly, or exchanging aged cells for cells which continue keeping the length of telomeres and telomerase activity is necessary. However, shortening of telomeres is not always said to dominate short lives of individuals completely, because shortening of telomeres in vivo is suppressed as compared with shortening of telomeres in vitro environment, and because telomeres of mice, whose maximum lives are three odd years, are longer than telomeres of human beings.

Somatic cells are, so to speak, the germ cells for asexual reproduction, since ontogeny is also possible from differentiated cells. And the germ–line cells for sexual reproduction undergo alternation of nuclear phases and zygoses. These cells which are differentiated for sexual reproduction and what is called " exceptionally preserved" become haploid n state by meioses from diploid 2n state. Then in fertilization both haploid n nuclei fuse to produce diploid 2n undifferentiated cells, in which these germ cells disappear. In brief, slightly differentiated cells for sexual reproduction with a view to turning into undifferentiated after all are brought back to the undifferentiated state in the place of eggs.

These germ cells which once disappeared in the undifferentiated cell

soon reappear as mesoderm in the gastrula stage. And at least in the fifth week of development primordial germ cells 7 14 appear, which hardly ever grow old. Individuals and clone bodies in themselves preserve these 2n germ–line cells, which continue maintaining telomerase activity despite repeating mitoses. Therefore, by using 2n germ–line cells, I can regenerate new cell age clone bodies, organs, tissues, cells, etc., with piling up inductive interactions according to polarities, concentration gradients, time passage, etc.

Including somatic cell clones and parthenogenesis, etc., there are relative relations between the differentiating state and the undifferentiated state, and both states are reversible and interconvertible each other. Cytoplasm of eggs reverses direction toward differentiation, extricates cells from the differentiated state, and induces nuclei of cells in the undifferentiated direction toward ontogeny again. It can be called resuscitation that cells getting to compose tissues and organs as a result of differentiation regain every possibility once more. This rejuvenating nature of eggs newly brings back the old age of cells walking through senility toward death, and newly recovers structures and functions of cells. That is to say, nuclei respond to messages from cytoplasm. As DNA itself is stored, DNA expressions change. Nuclear components such as DNA preserved in resuscitated cells dispatch messages. And this time components in cytoplasm respond to these messages. Nuclei as well react reciprocally, receiving messages from cytoplasm. Fibrous cytoskeletons running in all directions through cytoplasm are a series of tubes connecting plasma membranes and nuclear envelopes. These cytoskeletons operate from plasma membranes to nuclei together and begin new divisions.

That cells are worn out with age means that efficiency of metabolism, that is, the turnover of substances in organelles, is getting worse and wastes accumulate. Even in animal cells without vacuoles waste matters adhere and repairing processes become hard to operate. Physically it comes to be impossible for old cells to keep their sizes and shapes on the earth.

Lives have continued to the present and have been changing by

successions and diffusions of physical and chemical stimuli from time immemorial. Through plasma membranes, stimuli from the outside, either directly, or some of which have been converted into new physical and chemical stimuli inside the cell, have great influences on structures and functions of genes quantitatively. The range of environments, such as temperature, air, water, etc., where terrestrial creatures survive, is not so wide. Environments where terrestrial creatures can develop, as well, are restricted within a certain narrow limit. And, from among variously changing genes, the genes which can retain cell homeostasis are preserved.

DNA is not the only substance that is preserved. By sexual reproduction DNA moves from one individual to another individual. Inside the individual DNA is preserved by asexual reproduction. However, including mitochondria, structures and functions of cytoplasm are also preserved in eggs originally. Organelles scattered in nuclei and cytoplasm are preserved by asexual reproduction in the individual. Furthermore, structures and functions of cytoplasm are, in addition to asexual reproduction in the individual, preserved by eggs in sexual reproduction. On the material level each organella can exist independently. When these organelles construct buildings called cells, each organella takes up its suitable position. In the place, namely where eggs are formed, by physical and chemical stimuli such as fertilization, etc., organelles which have gotten their appropriate positions advance reactions which grow to chain flows accompanying the passage of time with a great many of vectors. And then, proliferating cells swimming with the current of differentiation in themselves increase and assemble. These proliferating cells migrate to their positions, stick to their positions, and form tissues, organs, and individuals.

Each cell that is growing old can at any time return to the undifferentiated state by rejuvenating nature of egg cytoplasm. As well, by hybridization and parthenogenesis of individuals and clone bodies, I can create newly–regenerated clone body groups which have new undifferentiated cells. These cells do not have the consciousness of oneself with which individuals are possessed. With using newly–regenerated cells produced by

making the most of these many clone body groups of various levels, I can regenerate tissues, organs, individuals, etc., in the condition of young and fresh cell age. This invention can separate differentiation from time passage.

There are various ways of sex determination. I can use my invention practically according to these ways of sex determination. There are also hermaphrodite organisms, in which each individual has both male and female reproductive systems, such as most sponges, flatworms, tapeworms, etc. Some hermaphrodites fertilize themselves. This is one way to create newly-regenerated clone bodies. In some species like Caribbean bluehead wrasses the sequential hermaphrodite is protogynous, while other species such as oysters are protandrous. Sex reversal can be induced by temperature effects on the production of male or female zygotes in some turtles. And chromosomal basis of sex varies with the organism. I will take some instances.

1. The X-Y system. The sex of an offspring depends on whether the sperm cell has an X chromosome or a Y chromosome in humans, dogs, cats, cattle, horses, killifish, fruit flies, etc.

2. The X-O system. In longheaded locusts, dragonflies, Emma field crickets, grasshoppers, roaches, etc., there is only one type of sex chromosome, namely the X chromosome. Males are XO. Males have only one sex chromosome, and the O means zero. Females are XX. Sex of the offspring is determined by whether the sperm cell carries an X chromosome or no sex chromosome.

3. The Z-W system. In chickens, ringed snakes, silk moths, etc., the variable that determines sex is the sex chromosome present in the ovum. The sex chromosomes are designated Z and W. Males are ZZ and females are ZW.

4. The Z-O system. There is only one type of sex chromosome, that is, the Z chromosome, in green turtles, Psychidae, pigeons, lizards, etc. Males are ZZ. Females are ZO. Females have only one sex chromosome. Sex of the offspring is determined by whether the ovum contains an Z chromosome or no sex chromosome.

5. The haplo-diploid system. There are no sex chromosomes in most species

of bees and ants. Females develop from fertilized ova and are thus diploid. Males develop from unfertilized eggs and are haploid.

The significance in my invention

In this way, my invention newly regenerate life age of individuals, clone bodies, organs, tissues, cells, etc. By using germ–line cells in individuals and clone bodies of creatures, I regenerate new cell age clone bodies, organs, tissues, cells, etc. Thus, I can maintain young and healthy individuals permanently. As well, by using the rejuvenating nature of eggs, I can renew old cells. Moreover, by joining crossable and fertile closely–related species to newly–regenerated clone body groups, and as well, with these closely–related species, preserved DNA, RNA, germ cells, etc., I can resurrect ancient creatures. By replacing old organs, such as cells, tissues, organs, etc., with newly–resuscitated healthy regenerated organs, such as cells, tissues, organs, etc., of the same gene types, I resuscitate various cells, tissues, organs, etc. By this method, I can resuscitate the whole individual. And I can continue reincarnating creatures eternally. That is to say, creatures continue resetting their life time while they are living on without death. With integrating the use of artificial materials and new energy systems together into these repeated processes, I can more and more improve the performance of cells, tissues, organs, etc. And I can create diversely evolving lives with undergoing remarkable changes in themselves.